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PROJECT ADMINISTRATION DATA SHEET

[x] ORIGINAL [ ] REVISION NO. _____

Project No. E-16-645 (subproject is E-23-625/Vito/ESM) DATE 4/1/82

Project Director: Don P. Giddens School/Lab ~~4/1/82~~ AE

Sponsor: National Science Foundation; Washington, D. C.

Type Agreement: Amend 02 to Grant MEA-7921551 (formerly CME-7921551)

Award Period: From 2/15/82 To 8/31/83 (Performance) _____ (Reports)

Sponsor Amount: $127,936 (Amend 02 only) * Contracted through:

Cost Sharing: $15,643 (E-16-372) GTRI/GIT

Title: Role of Fluid Mechanics in the Genesis, Proliferation and Detection of Atherosclerosis

ADMINISTRATIVE DATA OCA Contact Leamon R. Scott JOHN BURDETTE

1) Sponsor Technical Contact:

George K. Lea
National Science Foundation
Fluid Mechanics Program
Mechanical & Engineering Group
Civil & Mechanical Engineering
Washington, D. C. 20550
202-357-9542

2) Sponsor Admin/Contractual Matters:

Terry J. Pacovsky
National Science Foundation
Division of Grants & Contracts
Award Accountability Branch
Washington, D. C. 20550
202-357-9626 SEE REVISION

Defense Priority Rating: N/A Security Classification: N/A

RESTRICTIONS

See Attached NSF Supplemental Information Sheet for Additional Requirements.

Travel: Foreign travel must have prior approval — Contact OCA in each case. Domestic travel requires sponsor approval where total will exceed greater of $500 or 125% of approved proposal budget category.

Equipment: Title vests with GIT

COMMENTS:

Continuation of E-16-664. New Project number assigned due to change in O.H. computation.

* $123,077 in E-16-645 and $4,859 in E-23-625.

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SPONSORED PROJECT TERMINATION/CLOSEOUT SHEET

Date 8/2/84

Project No. E-16-645 School/Lab AE

Includes Subproject No.(s) E-23-625 /Vito/ESM

Project Director(s) Don P. Giddens GTRI / ~~GTL~~

Sponsor National Science Foundation

Title "Role of Fluid Mechanics in the Genesis, Proliferation and Detection of Atherosclerosis"

Effective Completion Date: 10/31/83 (Performance) 1/31/84 (Reports)

Grant/Contract Closeout Actions Remaining:

- [ ] None
- [x] Final ~~Project Cost Final Fiscal~~ Report FCTR
- [ ] Closing Documents
- [x] Final Report of Inventions if positive
- [x] Govt. Property Inventory & Related Certificate if positive
- [ ] Classified Material Certificate
- [ ] Other _____

Continues Project No. E-16-664 Continued by Project No. _____

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APPENDIX VII

E-16-645 and E-16-664 (continued by 645)

NATIONAL SCIENCE FOUNDATION
Washington, D.C. 20550

FINAL PROJECT REPORT
NSF FORM 98A

PLEASE READ INSTRUCTIONS ON REVERSE BEFORE COMPLETING

PART I–PROJECT IDENTIFICATION INFORMATION

1. Institution and Address	2. NSF Program	3. NSF Award Number
Georgia Institute of Technology Atlanta, Georgia 30332		MEA - 7921551
	4. Award Period From 2/15/82 To 10/31/83	5. Cumulative Award Amount $388,809

6. Project Title

Role of Fluid Mechanics in the Genesis, Proliferation and Detection of Atherosclerosis

PART II–SUMMARY OF COMPLETED PROJECT *(FOR PUBLIC USE)*

The research program was designed to determine which fluid dynamic factors relate to the development of atherosclerotic lesions in animal models and in human subjects by correlating various possible factors with lesion localization in specific arteries. Research methods combined both engineering and biological scientific personnel and techniques. Fluid dynamic studies in models of the human carotid bifurcation and of vessels with localized constrictions were performed at the Georgia Institute of Technology using laser Doppler anemometry to measure the velocity field. Animal studies were carried out using pulsed Doppler ultrasound to measure blood velocities in vivo. For the biological studies at the University of Chicago Medical School, constrictions were placed on the aortas of cynomolgus monkeys which were then fed an atherogenic diet for six months, after which the pattern of lesion development was examined morphologically. Investigations were also performed on excised carotid bifurcations from fresh cadavers, and the intimal and medial thicknesses were measured as a function of location within the vessels. The pathologic and fluid dynamic findings were then correlated. Results show that high wall shear and turbulence, both postulated in the literature as causative hemodynamic factors, are not causes of atherogenesis in either the animal model or the human carotid vessels. Rather, lesion development coincided with specific regions where wall shear was low in magnitude and/or where the direction of wall shear oscillated significantly during the heart cycle.

PART III–TECHNICAL INFORMATION *(FOR PROGRAM MANAGEMENT USES)*

1. ITEM *(Check appropriate blocks)*	NONE	ATTACHED	PREVIOUSLY FURNISHED	TO BE FURNISHED SEPARATELY TO PROGRAM	
				Check (√)	Approx. Date
a. Abstracts of Theses					
b. Publication Citations					
c. Data on Scientific Collaborators					
d. Information on Inventions					
e. Technical Description of Project and Results					
f. Other *(specify)*					

2. Principal Investigator/Project Director Name *(Typed)*	3. Principal Investigator/Project Director Signature	4. Date
Don P. Giddens		7/23/84

NSF Form 98A (3-83) Supersedes All Previous Editions

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APPENDIX VII

NATIONAL SCIENCE FOUNDATION
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FINAL PROJECT REPORT
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PART I–PROJECT IDENTIFICATION INFORMATION

1. Institution and Address	2. NSF Program	3. NSF Award Number
Georgia Institute of Technology Atlanta, Georgia 30332		MEA - 7921551
	4. Award Period From 2/15/80 To 10/31/83	5. Cumulative Award Amount $388,809

6. Project Title

Role of Fluid Mechanics in the Genesis, Proliferation and Detection of Atherosclerosis

PART II–SUMMARY OF COMPLETED PROJECT *(FOR PUBLIC USE)*

The research program was designed to determine which fluid dynamic factors relate to the development of atherosclerotic lesions in animal models and in human subjects by correlating various possible factors with lesion localization in specific arteries. Research methods combined both engineering and biological scientific personnel and techniques. Fluid dynamic studies in models of the human carotid bifurcation and of vessels with localized constrictions were performed at the Georgia Institute of Technology using laser Doppler anemometry to measure the velocity field. Animal studies were carried out using pulsed Doppler ultrasound to measure blood velocities in vivo. For the biological studies at the University of Chicago Medical School, constrictions were placed on the aortas of cynomolgus monkeys which were then fed an atherogenic diet for six months, after which the pattern of lesion development was examined morphologically. Investigations were also performed on excised carotid bifurcations from fresh cadavers, and the intimal and medial thicknesses were measured as a function of location within the vessels. The pathologic and fluid dynamic findings were then correlated. Results show that high wall shear and turbulence, both postulated in the literature as causative hemodynamic factors, are not causes of atherogenesis in either the animal model or the human carotid vessels. Rather, lesion development coincided with specific regions where wall shear was low in magnitude and/or where the direction of wall shear oscillated significantly during the heart cycle.

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d. Information on Inventions	✓				
e. Technical Description of Project and Results		✓			
f. Other *(specify)*					

2. Principal Investigator/Project Director Name *(Typed)*	3. Principal Investigator/Project Director Signature	4. Date
Don P. Giddens		7/23/84

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ABSTRACT

AN EXPERIMENTAL INVESTIGATION OF STEADY FLOW
AT AN
ARTERIAL BIFURCATION

A PH.D. THESIS

BY

K. BALASUBRAMANIAN

The geometry of a typical adult human carotid bifurcation was established from a study of a large number of angiograms. A rigid model was constructed from glass and investigations were performed under steady flow conditions using dye injection and hydrogen bubbles. A second model was machined from plexiglas and employed in a series of laser Doppler anemometer measurements of velocity profiles within the bifurcation. Physiologic ranges of Reynolds numbers and flow division ratios were utilized in the experiments. The studies revealed a complex flow field in which flow separation and secondary flow patterns play an important role. The separation regions occurring at the outer regions of the branches are zones of low shear stress but are not regions of recirculation. The apex or flow divider neighborhood experiences relatively high wall shear stress while the side walls of the carotid sinus contain areas of moderate shear levels. Comparison with pathologic data for localization of atherosclerotic lesions indicates that zones susceptible to disease are areas which experience low shear stress while regions of relatively high shear are free of deposits.

ABSTRACT

AN EXPERIMENTAL INVESTIGATION OF STEADY AND PULSATILE FLOW THROUGH CONSTRICTED TUBES

A PH.D. THESIS

BY

S. A. AHMED

An experimental investigation of steady and pulsatile flow through axisymmetric contoured constrictions in a rigid tube has been conducted. The study was motivated by the problem of arterial stenoses occurring in certain cardiovascular diseases. Flow disturbances caused by the constriction have been shown to be an important feature of the flow, and their analysis may offer a diagnostic tool which could help in early detection of the disease.

Contoured constrictions with 25 percent, 50 percent and 75 percent area reductions were investigated. The steady flow experiments covered a range of Reynolds numbers from 500 to 2,000 while the pulsatile flow had an instantaneous Reynolds number varying from 200 to 1,000. The pulsatile upstream centerline velocity waveform was approximately sinusoidal with a frequency parameter of 7.5.

Investigations by flow visualization utilizing the hydrogen bubble technique demonstrated a complex flow field, particularly in the case of pulsating flow, consisting of a separated region downstream of the constriction, vortex shedding in the near distal region and turbulence in the far field.

Quantitative measurements of two velocity components made with a two-component laser Doppler velocimeter provided additional details on the development of velocity profiles, disturbance velocity profiles and wall shear stresses. Velocity measurements were conducted at numerous axial locations and radial positions.

The steady flow results show that the length of the laminar recirculation region increases with the Reynolds number and with the area reduction. Furthermore, the mean velocity profiles exhibit a jet-like character with large changes in velocity gradient. Downstream of the constriction, the flow field is dominated by vortex shedding which either breaks up into random fluctuations or decays deterministically due to viscosity effects, depending on the upstream conditions and stenosis geometry. Generally, disturbances are generated in the shear layer with a large fraction of the energy in the fluctuations being at lower frequencies. Nondimensional correlations were applied to the disturbance energy spectra.

The pulsatile flow is characterized by the lack of a stationary separated zone. Instead, there is a region of reverse flow which expands during systole and contracts during diastole. For high values of the frequency parameter, a strong vortex ring swirls into this region and is washed away during the next cycle. Flow disturbance analysis was applied to small intervals of the cycle to isolate the different fluid mechanics phenomena namely, starting coherent structure, vortex shedding and turbulence. The existence and interaction among these phenomena depend on the maximum Reynolds number, the frequency parameter and the degree of the constriction.

In general, the fundamental frequency of the velocity fluctuations increases with the degree of constriction at fixed axial location for both steady and pulsatile flows. However, it decreases farther downstream for the same occlusion.

Thus, the results of the present investigation have led to an extensive description of the flow field through a constricted tube with steady or pulsatile upstream flow conditions. The disturbances measured in the flow field are expected to help in the early detection of the initial formation of occlusions before becoming serious and clinically significant.

B. PUBLICATIONS

Papers and presentations listed in this section are directly related to the research areas of our present NSF Grant (February 15, 1980 - February 14, 1983). This listing does not include papers and presentations of the principals in other research areas.

A. Papers Published During NSF Grant Period and Related to NSF Research

1. A. M. A. Khalifa and D. P Giddens; "Characterization and Evolution of Poststenotic Flow Disturbances," Journal of Biomechanics, Vol. 14, No. 5, 1981, pp. 279-296.

2. B. K. Bharadvaj, R. F. Mabon, and D. P. Giddens; "Steady Flow in a Model of the Human Carotid Bifurcation: Part I-Flow Visualization," Journal of Biomechanics, Vol. 15, No. 5, 1982, pp. 349-362.

3. B. K. Bharadvaj, R. F. Mabon, and D. P. Giddens; "Steady Flow in a Model of the Human Carotid Bifurcation: Part II-Laser Doppler Anemometer Measurements," Journal of Biomechanics, Vol. 15, No. 5, 1982, pp. 363-378.

4. D. P. Giddens and A. M. A. Khalifa; "Turbulence Measurements with Pulsed Doppler Ultrasound Employing a Frequency Tracking Method," Ultrasound in Medicine and Biology, Vol. 8, No. 4, 1982, pp. 437-437.

5. R. I. Kitney, D. P. Giddens, and R. F. Mabon; "Flow Disturbance Analysis of Aortic Velocity Waveforms," In Blood Flow - Theory and Practice, Ed. D. Taylor, Pitman, Med., pp. 63-83.

6. R. I. Kitney and D. P. Giddens, "Extraction and Characterization of Underlying Velocity Waveforms in Poststenotic Flow," Institution of Electrical Engineers (IEE Proceedings), Part A, Special Issue on Biomedical Engineering, December, 1982.

7. D. N. Ku and D. P. Giddens; "Pulsatile Flow in a Model Carotid Bifurcation," Arteriosclerosis, Vol. 3, No. 1, 1982, pp. 31-39.

8. W. D. Wilcox, T. A. Carrigan, K. J. Dooley, D. P. Giddens, F. D. Dykes, A. Lazzara, J. L. Ray, and P. A. Ahmann; "Range-gated Pulsed Doppler Ultrasonagraphic Evaluation of Carotid Arterial Blood Flow in Small Preterm Infants with Patent Ductus Arteriosus," Journal of Pediatrics, Vol. 102, No. 2, 1983, pp. 294-298.

9. M. D. Deshpande and D. P. Giddens; "Computation of Turbulent Flow Through Constrictions," AICE Journal of Engineering Mechanics, Vol. 109, No. 2, 1983, pp. 466-478.

10. L. J. D'Luna, V. L. Newhouse and D. P. Giddens: "In Vitro Doppler Detection of Axisymmetric Stenoses from Transverse Velocity Measurements," Journal of Biomechanics, Vol. 13. No. 9, 1982, pp. 647-660.

11. S. A. Ahmed and D. P. Giddens; "Velocity Measurements in Steady Flow Through Axisymmetric Stenoses at Moderate Reynolds Numbers," Journal of Biomechanics, Vol. 16, No. 7, 1983, pp. 505-576.

12. C. K. Zarins, R. A. Bomberger, K. E. Taylor, and S. Glagov: "Artery Stenosis Inhibits Regression of Diet-induced Atherosclerosis," Surgery, 88:86-90, 1980.

13. R. A. Bomberger, C. K. Zarins, and S. Glagov; "Medial Injury and Hyperlipidemia in the Development of Aneurysms or Atherosclerotic Plaques," Surg. Forum, 31:338-340, 1980.

14. C. K. Zarins, E. J. DelBeccaro, L. Jones, J. K. Turcotte, and G. J. Dohrmann, "Increased Cerebral Blood Flow After External Carotid Artery Revascularization," Surgery, 89:730-734, 1981.

15. R. A. Bomberger, C. K. Zarins, and S. Glagov; "Subcritical Arterial Stenosis Enhances Distal Atherosclerosis," Resident Research Award, J. Surg. Res., 30:205-212, 1981.

16. S. Glagov, J. Grande, D. Vesselinovitch, and C. K. Zarins; "Quantitation of Cells and Fibers in Histologic Sections of Arterial Walls," In Connective Tissues in Arterial and Pulmonary Disease, Ed. T. F. McDonald and A. B. Chandler, Springer-Verlag, New York, pp. 57-93, 1981.

17. C. K. Zarins, R. A. Bomberger, and S. Glagov; "Local Effects of Stenoses: Increased Flow Velocity Inhibits Atherogenesis, Circulation 64 (Suppl. II): 221-227, 1981.

18. R. T. Lyon, C. K. Zarins, C. Lu, C. F. Yang, and S. Glagov; "Arterial Wall Disruption by Balloon Dilation: Quantitative Comparison of Normal, Stenotic and Occluded Vessels," Surg. Forum, 32:326-328, 1981.

19. C. K. Zarins and S. Glagov; "Aneurysms and Obstructive Plaques: "Differing Local Responses to Atherosclerosis," Aneurysms: Diagnosis and Treatment, Ed: John J. Bergan and James S. T. Yao, Grune & Stratton, Inc., New York, pp. 61-82, 1981.

20. C. K. Zarins, K. E. Taylor, R. A. Bomberger, and S. Glagov: "Do Endothelial Injuries Predispose to Atherosclerosis?" Angio 3:325-329, 1981.

21. A. G. Little and C. K. Zarins; "Abdominal Aortic Aneurysm and Behcet's Disease," Surgery 91:359-362, 1982.

22. S. Glagov and C. K. Zarins: "Natural History of Human Atherosclerotic Lesions: Changes in Luminal Configuration," Noninvasive Techniques for Assessment of Atherosclerosis in Peripheral, Carotid and Coronary Arteries, Ed. T. F. Budinger, A. S. Berson, I. Ringqvist, M. B. Mock, J. T. Watson and R. J. Powell, Raven Press, New York, pp. 15-19, 1982.

23. S. Glagov and C. K. Zarins; "Pathophysiology of Aneurysm Formation," Aneurysms, Ed. Morris Kerstein, Williams & Wilkins, Baltimore, MD, In Press.

24. S. Glagov and C. K. Zarins; "Quantitating Atherosclerosis: Problems of Definition," Noninvasive Diagnosis of Atherosclerotic Lesions: Quantitative Evaluation of Morphology, Biochemistry, and Pathophysiology, Eds. Drs. M. Gene Bond, William Insull, Jr., Seymour Glagov, J. Frederick Cornill and A. Bleakley Chandler, Springer-Verlag, New York, In Press.

25. C. K. Zarins, M. A. Zatina and S. Glagov; "Correlation of Postmortem Angiography with Pathologic Anatomy: Quantitation of Atherosclerotic Lesions," Noninvasive Diagnosis of Atherosclerotic Lesions: Quantitative Evaluation of Morphology, Biochemistry, and Pathophysiology, Eds. Drs. M. Gene Bond, William Insull, Jr., Seymour Glagov, J. Frederick Cornhill and A. Bleakley Chandler, Springer-Verlag, New York, In Press.

26. S. Glagov, C. K. Zarins, K. E. Taylor, R. A. Bomberger, and D. P. Giddens; "Evidence that High Flow Velocity and Endothelial Disruption are not the Principal Factors in Experimental Plaque Localization," In Proc. of Specialists' Meeting on Fluid Dynamics as a Localizing Factor in Atherosclerosis, Springer-Verlag, Heidelberg, (in press).

27. C. K. Zarins, D. P. Giddens, and S. Glagov; "Atherosclerotic Plaque Distribution and Flow Velocity Profiles in the Carotid Bifurcation," Cerebrovascular Insufficiency, Ed. John J. Bergan and James S. T. Yao, Grune & Stratton, Inc., New York, pp. 19-30, 1982.

28. C. K. Zarins, C. T. Lu, B. L. Gewertz, R. T. Lyon, D. S. Rush, and S. Glagov; "Arterial Disruption and Remodeling Following Balloon Dilatation," Surgery, 29:1086-1095, 1982.

29. S. Glagov and J. Clark; "A Unitary View of Arterial Medial Microarchitecture," Hemodynamics and the Arterial Wall, Proceedings from a Specialists Meeting, Houston, Texas, 1980, pp. 52-56.

30. R. W. Wissler, D. Vesselinovitch, T. J. Schaffner, and S. Glagov; "Quantitating Rhesus Monkey Atherosclerosis Progression and Regression with Time," Atherosclerosis V, Eds. A. M. Gotto, Jr., L. C. Smith and B. Allen, Springer-Verlag, New York, P. 757, 1980.

31. T. Schaffner, K. Taylor, C. K. Zarins, S. Glagov, and R. W. Wissler; "Foam Cells with Macrophage Properties: Characterization in Experimental and Human Atheromatous Lesions," 2nd International Symposium on Atherosclerosis, Vienna, 1980.

32. S. Glagov, J. Grande, D. Vesselinovitch, and C. K. Zarins; "Quantitation of Cells and Fibers in Histologic Sections of Arterial Walls; Advantages of Contour Tracing on a Digitizing Plate," Connective Tissues in Arterial and Pulmonary Disease, Ed. T. F. McDonald and A. B. Chandler, Springer-Verlag, New York, 981.

B. Papers Presented During NSF Grant Period and Related to NSF Research

1. R. I. Kitney, D. P. Giddens, and R. F. Mabon; "Flow Disturbance Analysis of Aortic Velocity Waveforms," Blood Flow-theory and Practice, BIO-ENG 80, London, March 1980.

2. D. P. Giddens; "Flow Disturbance Measurement with Pulsed Doppler Ultrasound," Association for the Advancement of Medical Instrumentation 15th Annual Meeting, San Francisco, April 1980. (Invited)

3. D. P. Giddens, K. Balasubramanian, and R. F. Mabon; "Steady Flow at the Carotid Bifurcation," 2nd Mid-Atlantic Conference on Biofluid Mechanics, Blacksburg, VA, May 4-6, 1980.

4. K. Balasubramanian, R. F. Mabon, and D. P. Giddens; "Flow in the Carotid Bifurcation," Specialists Meeting on Hemodynamics and the Arterial Wall, Ed. by R. M. Nerem and J. R. Guyton, Houston. November 5-7, 1980. (Invited)

5. K. Balasubramanian and D. P. Giddens; "Flow Studies at the Carotid Bifurcation," ASME 1980 Centennial Winter Annual Meeting, Chicago, November 1980.

6. M. Casty, D. P. Giddens, and M. Anliker; "Microprocessor Controlled Multigate Pulsed Ultrasound Doppler Technique for Quantitative Velocity and Flow Measurements," Joint ASME/ASCE Mechanics Summer Meeting, Boulder, CO, June 1981.

7. D. P. Giddens, C. K. Zarins, S. Glagov, R. F. Mabon, and D. N. Ku; "Acute and Chronic Flow Disturbances Due to Aortic Coarctation in Monkeys," Vascular Research Forum, Annual Meeting of the Society of Vascular Surgery and International Cardiovascular Society, Dallas, TX, June 1981.

8. M. Casty and D. P. Giddens; "25 + 1 Channel Multigate Pulsed Doppler Instrument for Profile, Flow and Turbulence Analysis in Major Arteries," Annual Scientific Meeting of the American Institute of Ultrasound in Medicine, San Francisco, CA, August 1981. (Plenary Sessions)

9. D. P. Giddens, C. K. Zarins, S. Glagov, R. F. Mabon, D. N. Ku, and M. Casty; "Flow Disturbances and Atherogenesis in the Monkey Aorta," 34th Annual Conference on Engineering in Medicine and Biology, Houston, TX, September 1981. (Invited)

10. D. P. Giddens and M. Casty; "Flow and Velocity Disturbance Measurements in Carotid Arteries," 34th Annual Conference on Engineering in Medicine and Biology, Houston, TX, September 1981.

11. D. N. Ku and D. P. Giddens; "Pulsatile Flow Visualization in a Carotid Bifurcation Model," 34th Annual Conference on Engineering in Medicine and Biology, Houston, TX, September 1981.

12. D. P. Giddens, C. K. Zarins, B. K. Bharadvaj, R. F. Mabon, and S. Glagov, "Fluid Dynamics and Plaque Localization in the Carotid Bifurcation," 1981 ASME Winter Annual Meeting, Washington, November 1981.

13. D. P. Giddens, C. K. Zarins, S. Glagov, B. K. Bharadvaj, and D. N. Ku; "Flow and Atherogenesis in the Human Carotid Bifurcation," Sixth International Atherosclerosis Symposium - Satellite Symposium on Fluid Dynamics as a Localizing Factor for Atherosclerosis, Heidelberg, June 1982. (Invited)

14. R. I. Kitney and D. P. Giddens; "Velocity Waveform Analysis in Poststenotic Flow," Third International Conference on Mechanics in Medicine and Biology, Compiegne, France, June 1982.

15. S. Ahmed, M. D. Deshpande, and D. P. Giddens; "In Vitro Stenotic Flows at Moderate Reynolds Numbers," 35th Annual Conference on Engineering in Medicine and Biology, Philadelphia, September, 1982.

16. T. A. Carrigan, W. D. Wilcox, and D. P. Giddens; "Early Detection of Patent Ductus Arteriosus with Ultrasound," 35th Annual Conference on Engineering in Medicine and Biology, Philadelphia, September, 1982.

17. D. P. Giddens and R. I. Kitney; "Flow Disturbances and Their Detection," San Diego Symposium on Noninvasive Diagnostic Techniques in Vascular Surgery, San Diego, October, 1982. (Invited)

18. W. D. Wilcox, T. A. Carrigan, K. J. Dooley, F. D. Dykes, A. Lazzara, and D. P. Giddens; "Range-gated Pulsed Doppler Ultrasonographic Evaluation of Carotid and Anterior Cerebral Blood Flow in Preterm Infants with Patent Ductus Arteriosus," 55th Scientific Sessions, American Heart Association, Dallas, November, 1982.

19. S. Glagov; "Microarchitecture of the Arterial Wall and the Pathogenesis of Arterial Disease," Symposium on Electron Microscope in Diagnosis and Research, Rush Medical School, Chicago, November, 1981.

20. S. Glagov; "Cell Pathology of Atherogenesis," State of the Art Council on Atheroschlerosis, American Heart Association, November, 1982. (Invited)

21. S. Glagov; "Atherosclerosis; The Problem of Definition," Workshop on Quantitative Atherosclerosis, Silver Spring, Maryland, February, 1982. (Invited)

22. S. Glagov; "Pathobiology of Atherogenesis," Symposium on Physiology and Pathophysiology of the Vessel Wall. Chairman and Keynote Talk, FASEB Meeting, April, 1982. (Invited)

23. S. Glagov, C. K. Zarins, and D. P. Giddens; "Evidence That High Flow Velocity and Endothelial Disruption Are Not the Principal Factors in Atherogenesis," Symposium of Specialists in Fluid Dynamics as a Localizing Factor in Atherosclerosis, Heidelberg, June, 1982. (Invited)

24. S. Glagov and C. K. Zarins; "Measurement and Identification of Atherosclerosis," Sixth International Symposium on Arteriosclerosis, Berlin, June, 1982.

25. C. K. Zarins and S. Glagov; "The Inverse Relationship Between Elevated Shear Stress and Plaque Localization," VI Hugh Lofland Conference, Winston Salem, North Carolina, April 29, 1981.

26. C. K. Zarins, D. P. Giddens, and S. Glagov; "The Influence of Flow Velocity on Endothelial Injury and Plaque Formation," Frederick A. Coller Surgical Society, Tuscon, Arizona, October 10, 1981.

27. C. K. Zarins, D. P. Giddens, B. K. Bharadvaj, and S. Glagov; "Carotid Plaques Localize in Regions of Low Flow Velocity and Shear Stress," American Heart Association, Dallas, Texas, November, 1981.

28. C. K. Zarins and S. Glagov; "Experimental Atherosclerosis; Differences Between Plaque Formation and Aneurysms," Northwestern Symposium on Arterial Aneurysms, Chicago, Illinois, December 10, 1981.

29. M. Zatina, C. K. Zarins, and S. Glagov; "Effect of Aortic Coarctation on Coronary Atherosclerosis," Society of University Surgeons 24th Annual Residents' Conference, New York, New York, February 10, 1982.

30. C. K. Zarins and S. Glagov; "Criteria for Anatomic Validation of Noninvasive Imaging Techniques," Proceedings of San Diego Symposium on Noninvasive Diagnostic Techniques in Vascular Disease, October, 1982. (Abstract)

31. D. P. Giddens and R. I. Kitney; "Flow Disturbances and Their Detection," Proceedings of San Diego Symposium on Noninvasive Techniques in Vascular Disease, October, 1982. (Abstract)

E. TECHNICAL DESCRIPTION OF PROJECT AND RESULTS

1. Hemodynamics and Atherosclerosis in the Human Carotid Bifurcation

In work accomplished in the laboratories of the School of Aerospace Engineering, the Georgia Institute of Technology, and the Departments of Surgery and Pathology, the University of Chicago, we have determined the following:

a. Atherosclerotic lesions in the human carotid bifurcation do not localize in regions of relatively high, unidirectional wall shear stress.

b. Although complex laminar secondary flow patterns occur in the normal carotid bifurcation, turbulence is not present until plaques are well-developed. Consequently, turbulence may influence the fate of established large plaques but can probably be ruled out as a direct initiating factor in atherosclerosis of the carotid artery.

c. Plaques localize in regions of the carotid bifurcation which experience a low mean wall shear stress (outer wall of the sinus) and in regions where the wall shear stress vector changes direction significantly during the cardiac cycle (outer wall and, to a lesser degree, side walls of the sinus).

d. Significant factors which affect flow patterns relative to (c) above are: branch angle, flow division ratio and flow pulse waveform.

As a result of these findings, turbulence and high, unidirectional wall shear stress do not appear to be initiating factors of atherosclerosis in the human carotid bifurcations. consequently. for future work we plan to concentrate upon investigating possible relationships between lesion localization and (i) specific characteristics of wall shear stress behavior and/or (ii) residence time of fluid elements near vessel wall sites susceptible to plaque development.

2. Stenotic Flows and Aortic Coarctations

The Departments of Surgery and Pathology (Drs. C. K. Zarins and S. Glagov) have many years experience with the cynomolgus monkey as an experimental model for atherosclerosis. In work performed during the present NSF funding we have studied a series of 11 monkeys (9 with coarctations and 2 without) which were placed on an atherogenic diet with 2% cholesterol and 25% peanut oil for a period of six months. At the time of implanting the coarctation, several hemodynamic variables were measured to characterize flow, pressure and flow disturbances in the aorta. At the time of sacrifice these measurements were repeated and particular attention was given to obtaining pulsed Doppler

ultrasound measurements in the poststenotic regions, concentrating primarily upon characterizing the intensity of flow disturbances induced by the constriction. Although we have not yet completed all our analyses of these data, we have determined the following to date:

a. Hypertension per se was not a consistent factor in the development of atherosclerosis in the monkey aorta.

b. Inasmuch as the coarctation channel itself was consistently spared, relatively high levels of unidirectional wall shear stress were considered to exert an inhibitory effect on atherogenesis.

c. A good correlation between turbulence intensity and disease sparing existed for several vessel diameters distal to the coarctation. Further distally, this correlation deteriorated significantly. Consequently, although we are not prepared to conclude that turbulent flow inhibited atherosclerosis, we can state that turbulence did not play a contributory role in these experiments.

All hemodynamic data are recorded on FM tape, and we will be continuing the analysis and correlation with pathology over the next several months.

Additionally, we have completed a series of contoured stenoses with area reductions of 25, 50 and 75%. Steady flow experiments at Re = 500, 1000 and 2000 were performed as well as pulsatile experiments which employed a sinusoidal waveform with minimum and maximum Reynolds numbers of 200 and 1000 and a frequency parameter of α = 7.5. These latter values are similar to those of the monkey aorta. We have not completed our analysis of these experiments nor have we yet related them to the monkey coarctation studies. However, the following conclusions have been drawn to date:

a. Detailed velocity profiles in steady and pulsatile flows have been obtained noninvasively with the LDA method. Results cover a range of transitional flows and can be employed for comparison with laminar and turbulent computational fluid dynamic models.

b. Wall shear stresses have been measured in the stenotic field. Values of τ_w are maximum within the throat of the constriction. In steady flow the separated flow region contains areas of low τ_w, but it also possesses areas for which the τ_w is comparable in magnitude, though opposite in direction, to the fully developed value far upstream.

c. The wall shear stress reaches a local maximum downstream of flow reattachment. However, this value is at most 2-3 times higher (when turbulence is present) than the upstream value, and it is an order of magnitude less than the maximum τ_w in the constriction throat.

d. Three distinct types of poststenotic disturbances can exist in pulsatile flow: (i) a coherent laminar structure associated with the acceleration phase of each cycle; (ii) laminar oscillations at discrete frequency arising from shed vortices; and (iii) turbulence.

Analysis of these data will continue over the next several months.